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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/732,241	12/07/2000	Mathai Mammen	P-095-R	9496

21186 7590 01/06/2005

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EXAMINER	
COVINGTON, RAYMOND K	
ART UNIT	**PAPER NUMBER**
1625	

DATE MAILED: 01/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/732,241	KWAK ET AL.	
	Examiner	Art Unit	
	Raymond Covington	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *5/26/04,16 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26,28-34 and 36-52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-26,28-34 and 36-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Claim 47is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claim is self-conflicting because the claim is drawn to pharmaceutical compositions without a dosage limitation. Please note that a pharmaceutical composition by definition cannot be either ineffective or toxic. Therefore a pharmaceutical composition without any dosage is self-conflicting. It is recommended that the term "therapeutically effective amount" be incorporated into the claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 48-49 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention is the method of treating disease by mediating muscarinic receptors in a mammal.

The state of the prior art is that it involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific disease). There is no absolute predictability and no established correlation between in vitro activity and the treatment of treating disease by mediating muscarinic receptors conditions such as cognitive disorder, as the in vitro data is not a reliable predictor of success even in view of the seemingly high level of skill in the art. The existence of these

obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

The specification lacks sufficient variations of operable examples of compounds where, for example, Rx is heteroaralkyl, R^2 is formula (I) n1 is 1, which would provide guidelines as to how to pick and choose compounds having the claimed utility.

While screening and assay may indicate that compounds encompassed by the claims have efficacy in inhibiting retroviral activity, it does not necessarily follow that the compounds have efficacy in treating the "cause" of a specific disease i.e. the disease per se. (See Cecil medical textbook p.1937-1938).

The presence or absence of working examples:

In addition, there is no proof that the claimed compounds or compositions have ever been administered to a human or to an animal model. The obstacles to therapeutic approaches and vaccine development in humans are well documented

in the literature. See, for example, Huff {J. Med. Chem. 34(8) 1991, p. 2305-2314} on page 2314.

There are insufficient exemplifications to support the treatment of all known diseases mediated by muscarinic receptors. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting a treatment or therapeutic regimen on its face. In order to provide proof of utility with regard to drugs and their uses, either clinical in vivo or in vitro data correlative to in vivo applicability or a combination of these can be used. However, the data must be such as to convince one of ordinary skill in the art that the proposed utility is sufficiently established as set forth in full, clear and exact terms in the disclosure. When the utility is directed to humans, the data must generally be clinical, however, adequate animal data would be acceptable in those instances wherein one of ordinary skill in the art would accept correlation to human utility. Thus, in order to rely on animal data, there must exist an art recognized animal model for testing purposes. In re Hartop, 311 F.2d 249, 135 USPQ 419 (CCPA 1962).

The claims are drawn to the treatment of any and all diseases mediated by muscarinic receptors with compounds of claim 1.

The quantity of experimentation needed is undue. One skilled in the art would need to determine what muscarinic receptor mediated conditions out of all such known conditions would be benefited by compounds of claim 1 and then would further need to determine which of the claimed compounds would provide treatment of the disease.

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad method recited in applicants' claims. As a result necessitating one of ordinary skill to perform an exhaustive search for which diseases can be treated by which compounds in order to practice the claimed invention.

> Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Claims directed to mediating a biochemical pathway are devoid identifiable utility and are therefore not useful unless the pathway at issue is

critical to treating some condition and the pathway modification and disease treatment are inexorably linked by factual evidence, a claim to the pathway modification is devoid of utility.

Nor are the claims included in vitro elements, its biological measurable outcome i.e. a critical result of a measurable biochemical pathway. Such claims failed to achieve the advantage over any basic physiological variations thus are not useful as required by 35 USC 101. (Splendor form Brassiers Inc. v. Rapid American corp., 187 USPQ 158). Provision of 35 USC 112 first paragraph will be met in regard to the requirement of "how to use" the claims when the statement of utility contains within it a succinct connotation of how to use the material or the art will recognized that standard means of administration are contemplated. ln re Johnson 127 USPQ 216,* ln re Hichings 144 USPQ 637. As it has been clearly explained the claims are devoid of measurable outcome of the biochemical pathway as to achieve any advantage over any basic physiological variations nor the claims provided target dosage or steps to carry out the process, thus are devoid of "how to use" requirement.

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, one of ordinary skill in the art would have to engage in undue experimentation to test which

diseases can be treated by the compounds of the instant claims, with no assurance of success.

Claims 1-23, 26, 28-34, 36-50 and 51 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The mix and match of combinations of variables lacks antecedent basis, description and enabling support from the specification.

Claim 46 recites the limitation "as described in Table A and Table B" in line one. There is insufficient antecedent basis for this limitation in the claim.

Claims must, under modern claim practice, stand alone to define an invention, and incorporation into claims by express reference to the specification is not permitted. *Ex parte Fressola*, 27 USPQ 2d 1608 (1993).

Claim 46 refers to Tables. There is insufficient antecedent basis in the claims for the Tables cited in the claims. It is improper for claims to refer to subject matter not contained therein, even if the subject matter is contained in the specification. It is suggested that Applicant delete the references to the Tables in each occurrence in the claim.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

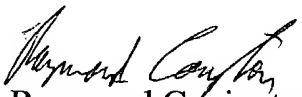
Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 24-26 and 51 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 3 of U.S. Patent No. 6,693,202. Although the conflicting claims are not identical, they are not patentably distinct from each other because piperdine compounds of the type recited in the claims. See, for example, claim 1 column 594 formula in line 35, column 598 lines 15-20 line 33-34.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Raymond Covington whose telephone number is (571) 272-0681. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, C. Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Raymond Covington
Examiner
Art Unit 1625

RKC